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RAYNAUD'S SYNDROME ; ACROSCLEROSIS ; SCLERODERMA.

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THE relation of Raynaud's syndrome to diffuse scleroderma of the acrosclerosis type, with predominance of sclerodactylia, evokes particular interest since this kind of scleroderma is often accompanied by Raynaud's syndrome ; occasionally it is preceded by the latter by many months or exceptionally by even several years. On the other hand, in the course of long-standing Raynaud's disease the skin of the hands becomes indurated, the changes resembling scleroderma, but with no tendency to spread and, in our opinion, not related to true scleroderma. The problem is highly complex and cannot be solved by morphological criteria alone, particularly in the early stages of scleroderma.

In cases of long-standing Raynaud's disease the skin of the fingers becomes oedematous, indurated, stiffened and atrophied ; occasionally, there is a resorption of the distal phalanges with attendant trophic disturbances of the nails. Estimates of the frequency of these changes vary ; according to Ormsby and Montgomery (1954) they occur in about 10% of Raynaud's disease cases, but Ratschow (1953) says that in the ultimate stage of Raynaud's disease almost all patients develop sclerodactylia. The essential differences between this and true scleroderma are that scleroderma runs a progressive course, i.e., spreads on the extremities from distal to proximal parts and also on the face; there are often telangiectases, various types of hyperpigmentation and depigmentation, and involvement of muscles, bone (osteoporosis, arthritis deformans), the alimentary tract, larynx and lungs.

This form of scleroderma was described by Hutchinson in 1893 as acrosclerosis, i.e. a combination of Raynaud's phenomenon with scleroderma of hands, face, and other regions. The recognition of scleroderma with vascular manifestations is based on the presence of angiospastic symptoms which often

precede sclerodermatous changes, and on the characteristic distribution of the skin changes predominating on the distal parts of the extremities. O'Leary and Nomland (1930) found sclerodactylia and vascular manifestations in 89% of diffuse scleroderma in a total of 48 cases. Brown, O'Leary and Adson (1930) reported that in 9 of 16 observed cases Raynaud's phenomenon preceded sclerodermatous changes, in 4 it coincided with the latter, and only in 3 cases there were no vascular symptoms at all.

Acrosclerosis was defined more exactly by Sellei (1931, 1936). He described acrosclerosis as an angiotrophoneurosis of face and hands and thought it to belong neither to the group of scleroderma nor to that of Raynaud's disease. The basic and primary symptoms of acrosclerosis are, according to Sellei, spasm of arterioles with cyanosis, very much resembling Raynaud's disease; necrosis, ulceration, changes in the bones and decalcification are secondary trophic lesions. Sellei believes that the essential difference between acrosclerosis and Raynaud's disease is that in the latter there is the characteristic gangrene, absence of which precludes—in his opinion—a definite diagnosis, with no induration of skin and deeper tissues of the hands, nor changes in the face. Sellei's description of acrosclerosis perfectly fits the concept of progressive diffuse scleroderma. He defines scleroderma as a local lesion of the connective tissue of the skin and of the subcutaneous tissue, possibly involving also more deeply situated tissues (muscles). Thus, Sellei admits as true scleroderma chiefly the circumscribed type, and of the generalized type only the widespread cases not confined to the extremities.

Sellei's views have gained wide acceptance and are quoted by many prominent authors (Ratschow, 1953, 1956). O'Leary and Waisman (1943) restrict the term acrosclerosis to cases in which Raynaud's syndrome precedes, or coincides with, scleroderma and in which the sclerodermatous changes do not spread rapidly. This approach excludes clinically identical cases in which there was originally no Raynaud's phenomenon—according to the authors one quarter of scleroderma cases—as well as rapidly spreading cases, irrespective of the prior existence of Raynaud's syndrome.

Allen, Barker and Hines (1946) prefer the name " acroscleroderma " in order to emphasize that it is a variety of scleroderma. They distinguish between acroscleroderma with concomitant Raynaud's syndrome (diffuse scleroderma with prevalence of changes in the extremities, or restricted merely to the hands of the sclerodactylia type, with Raynaud's syndrome) on the one hand and diffuse scleroderma without Raynaud's syndrome on the other. As a third group they distinguish sclerodactylia, but they do not give a closer definition of its nature. This nomenclature is no doubt justified since it stresses the connection with scleroderma, while the prefix " acro " indicates that the changes involve chiefly the distal parts of the extremities.

Changes in the skin, muscles, bones and inner organs leave no doubt that

acrosclerosis or acroscleroderma belongs to the group of sclerodermas, an opinion shared by American authors (Butler and Laymon, 1937 ; Wise, 1937). Doubts may be evoked by very early or abortive cases in which Raynaud's syndrome is accompanied by changes of the sclerodactylia type involving chiefly or exclusively the skin of the hands. In such cases it is very difficult, and on clinical criteria often impossible to tell whether it is a pseudoscleroderma attending Raynaud's disease or the beginning of a progressive acroscleroderma.

The clinical difference is chiefly in the extent of induration ; in Raynaud's disease sclerodermatous changes are principally restricted to the fingers, involving rarely the entire hand, and do not spread proximally whereas in scleroderma they are progressive. This criterion is of great importance in more advanced cases, or when prolonged observation of the patient is possible ; when the induration in early scleroderma involves only the hands, a decision becomes extremely difficult. Certain accessory clues are provided by the fact that in scleroderma, often even in a very early stage, there are at least abortive changes in the face ; further, in Raynaud's disease sclerodactylia occurs only after several years, whereas in scleroderma the vascular symptoms precede scleroderma by several, but rarely more than twenty, months. However, these criteria are unreliable whereas an early diagnosis is important, e.g., for deciding upon the advisability of sympathectomy.

According to O'Leary and Waisman, it is impossible to make this decision in one quarter of the cases and they consequently include in the acrosclerosis syndrome the sclerodermatous changes which develop in the hands in long-standing Raynaud's disease. This view, based on purely morphological premises, does not appear to be justified ; it is also opposed by Allen, Barker and Hines (1947).

In cases where clinical diagnosis is difficult, a decisive clue may be afforded by function tests and particularly by determination of sensory chronaxy of the skin.

In earlier investigations we demonstrated (Jablonska, 1953 ; Bubnow, 1955 ; Jablonska *et al.*, 1957) that in scleroderma sensory chronaxy is prolonged both in affected skin and, which is far more important, in the seemingly unchanged skin. This is pathognomonic for both diffuse and circumscribed scleroderma and occurs in no other disease, thus providing a distinction from scleroderma-like changes. In normal conditions, sensory chronaxy values vary between 0·1 and 0·6–0·8 sigma, depending on the site. In various skin diseases the chronaxy is prolonged in the skin lesions, depending upon the morphological character of the changes. Only in scleroderma, circumscribed as well as diffuse, is it prolonged in the seemingly healthy skin, and in the lesions much more so than in other diseases. In diffuse scleroderma, chronaxy is prolonged in the lesions to from 2·5 to 10 sigma, and varies in the seemingly healthy skin between 1·5 and 7 sigma. In circumscribed scleroderma, the indices are usually lower : Within the foci between 1·5 and 7 sigma, in the healthy

skin between 1 and 5 sigma, mostly not exceeding 3·5 sigma (Jablonska *et al.*, 1957).

In long-standing Raynaud's disease with sclerodermatous changes in the hands, clinically indistinguishable from sclerodactylia, chronaxy is prolonged in the affected skin but this is of no significance since it depends only on the morphological character of the lesion ; but it is absolutely normal in the rest of the skin, whereas in sclerodactylia, even when this is restricted to the skin of the fingers, and even when induration is much less pronounced, it is prolonged over the entire surface of the body. This is of decisive diagnostic value.

An illustration is provided by the following cases :

Case 1.—A woman aged 48 called at the department complaining of hardening and stiffening of skin of the hands. She had suffered from Raynaud's disease for 20 years. At first, cyanosis, pallor and oedema of the fingers were temporary and left no permanent trace. During the last ten years oedema persisted and induration of the fingers became increasingly pronounced.

The changes were very much like those of sclerodactylia—so much so that they could not be distinguished clinically from the latter.

A decisive clue was provided by measurements of chronaxy which was found to be normal in the healthy skin and only slightly prolonged in the distal parts of the hands (1·2 sigma).

Case 2.—As a comparison, we may mention a case of acroscleroderma which was morphologically identical or, at least, very similar. However, when first measured in 1953, chronaxy was prolonged in the areas involved to between 3·0 and 3·5 sigma, and varied in the unchanged skin between 1·5 and 2·5 sigma. After a year chronaxy was further prolonged and is now between 4·5 and 7·0 sigma in the seemingly healthy skin, and between 7·0 and 10·0 sigma in the hands. Continuously controlled, the chronaxy indices proved in Case 1 to remain at a constant level, i.e., normal in the unchanged skin.

Case 3.—The difficulties in diagnosis according to clinical criteria were still more evident in a third case, in whom the changes consisted chiefly of oedema and slight induration, the latter being less pronounced than in the case of a prolonged Raynaud's disease. Chronaxy was found to be prolonged in this patient over the entire skin, though seemingly normal, and this made it possible to diagnose progressive scleroderma restricted to the hands.

Capillaroscopy is also of some accessory value, for it reveals two entirely different pictures in Raynaud's disease and in diffuse scleroderma. In Raynaud's disease the capillary loops are very dilated and enlarged, with irregular indentate outlines and aneurysmal dilatations of the walls (Fig. 1). The blood stream is very slow and stasis always distinct. Vascular reactions to physical stimuli are notably reduced.

In scleroderma, the number of loops is substantially decreased, the capillaries are markedly deformed, and occasionally only parts of loops are visible. They are distributed irregularly in the microscopic field, on a very pale background. The blood stream is slow, beaded, with frequently visible large gaps (Fig. 2). Reactions to physical stimuli are usually suppressed. These findings in scleroderma differ from the descriptions given by Brown and O'Leary (1925) and by

Brown, O'Leary and Adson (1930) who found wide, irregular loops with indentate outlines, resembling the capillaries in Raynaud's disease. We suspect that these authors were dealing with acroscleroderma coinciding with Raynaud's syndrome ; in such cases our examinations revealed changes identical with those described (Fig. 3).

Capillaroscopy revealed distinct differences between scleroderma without Raynaud's syndrome and scleroderma coinciding with the latter. In the second type of case however, the capillaroscopic picture differs from that found

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

in an abortive Raynaud's disease or in Raynaud's phenomenon of a different origin (Fig. 4), since the capillaries, which are not dilated, are here very thin, contracted and deformed, their reactions being suppressed.

The capillaroscopic picture is somewhat different in cases of pseudoscleroderma tous change in Raynaud's disease of very long duration. Angiospastic changes of the arterioles over many years and proliferation of collagen obliterate the lumina of capillaries by strangulation, so that some of the loops are deformed, shortened and thin, and the blood stream is slow and beaded (Fig. 5). However, these changes are never so pronounced as in true scleroderma with concomitant Raynaud's syndrome (Fig. 3) ; and most of the loops show none of the typical dilatation of the central part, nor indentation and aneurysms of the capillary walls and the distinct increase in size which are typical of Raynaud's disease.

That the sclerodermatous changes in the fingers in cases of long-standing Raynaud's disease are distinct from true scleroderma is confirmed also by the histological picture. In Case 1 examination of the digital pulp revealed a very marked hypertrophy of the whole epidermis—pronounced hyperkeratosis, granulosis, acanthosis and papillomatosis. In the corium, apart from proliferation of the fibrous connective tissue, there was no sclerosis and homogenization of collagen which is so characteristic of scleroderma. The lumina of capillaries were as a rule reduced and around the vessels there were minimal inflammatory infiltrations. The sweat glands were numerous and showed no abnormality.

In this type of case histological examination is of little practical value since biopsies are not easily made on sclerosed fingers. The results are of interest, however, as they furnish further evidence of difference as compared with true acroscleroderma restricted to the fingers.

Fig. 5.

The clinical features and the progress of scleroderma with prevalent changes in the upper extremities and without Raynaud's syndrome are the same as in cases with Raynaud's phenomenon. They differ, however, from " acrosclerosis ", as understood by Hutchinson and Sellei, merely by absence of concomitant Raynaud's syndrome. Chronaxy in the seemingly unchanged skin proves characteristically prolonged. Capillaroscopy reveals the deformation and reduced numbers of loops typical of scleroderma, a slower blood stream and an almost complete absence of vascular reactivity.

The term " acrosclerosis " cannot be dissociated from scleroderma. The appearance of Raynaud's phenomenon is secondary and probably results from angioneurotrophic disturbances which are an essential element in the pathogenesis of scleroderma. According to Brown, O'Leary and Adson (1930), it is useful to distinguish this variety of scleroderma as acroscleroderma merely because sympathectomy is indicated only in such cases. Nowadays, sympathectomy having been discarded in principle in the treatment of scleroderma, while still carried out with success in Raynaud's disease, early differential diagnosis is of great importance. A means of early differentiation is provided

by determination of sensory chronaxy which is therefore of decisive importance in these cases.

Results and Conclusions.

In the course of long-standing Raynaud's disease there may develop sclerodermatous changes of the hands, identical with the initial stage of diffuse scleroderma.

Differentiation between scleroderma-like changes in Raynaud's disease and early scleroderma (sclerodactylia), very difficult or even impossible on clinical criteria, is based on the measurement of sensory chronaxy. Even in the earliest stage of scleroderma, this is prolonged not only on the sites involved, but also in the seemingly normal skin of the entire body. This is pathognomonic of scleroderma.

The disease described by Hutchinson as " acrosclerosis " was studied in more detail by Sellei who separated it from Raynaud's disease and scleroderma and defined it as an angiotrophoneurosis. Our investigations lead us to conclude that it is in fact a typical diffuse scleroderma, with prevalent changes in the upper extremities and face, coinciding with Raynaud's phenomenon.

The term " acroscleroderma " is much better than acrosclerosis since it indicates a connection with scleroderma. However, it does not seem useful to restrict the term " acroscleroderma " to cases in which Raynaud's phenomenon precedes the development of scleroderma and in which the disease runs a slow course.

The distinction between acroscleroderma with and without concomitant Raynaud's phenomenon can be accepted in principle, but there are no essential differences between the two varieties ; they run an identical course and Raynaud's phenomenon may appear at any stage or even remain altogether absent.

In the diagnosis of scleroderma with concomitant Raynaud's syndrome capillaroscopy is also valuable.

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AN EARLY RENAL LESION IN SYSTEMIC LUPUS ERYTHEMATOSUS.

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The renal lesion in systemic lupus erythematosus has been described in some detail on several occasions, notably by Klemperer, Pollack and Baehr (1941). These authors stressed the importance of the " wire loop " lesion in the capillary tuft of the glomerulus which they found in a high proportion of kidneys involved in systemic lupus erythematosus. They also described a focal necrotic lesion usually affecting the periphery of the glomerular tuft, which could occur in the absence of " wire loops ". Kark, Muehrcke, Pirani and Pollak (1955) in reviewing renal biopsy material in 32 patients, briefly described small localised areas at the periphery of the glomerulus, consisting of cellular proliferation.

In the present case, a renal biopsy presumably very early in the stage of renal involvement shows a focal cellular proliferation affecting only scattered glomeruli sometimes associated with focal necrosis.

Case Report.

An unmarried woman of 44 years first attended another hospital about 20 years ago with diffuse joint pains and an apparently classical Raynaud's phenomenon affecting the hands.

The patient first attended the dermatological outpatient department at St. Mary's Hospital in 1946 at the age of 33, with skin lesions affecting the lips, hands and arms, which subsequently cleared. In 1948 she was admitted to hospital with widespread erythematous lesions on the hands, forearms and upper lip. There was some atrophy and a contraction of the skin of the fingers. E.S.R. (Westergren) was 30 mm. in the first hour. Skiagram of the lungs showed no abnormality. She was treated with vitamin A 100,000 units daily and infra-red to the hands. There was very considerable improvement during the next month, but a raised E.S.R. (24) and erythematous lesions persisted on discharge.

The patient remained well in herself without any major alteration in the skin until November 1956, when she developed malaise and a pain in the right side of the chest on inspiration, with dyspnoea.

On admission, 7.xii.56, she was an ill woman with an intermittent temperature up to 102·5° F. The skin lesion had not altered markedly, typical erythematous lesions still being present on the circumoral region and forearms and hands, with atrophy and telangiectases about the nail folds. Also there were a few shallow ulcers on the buttocks. Enlarged lymph glands were palpable in the neck. B.P. 140/80. The joints of the fingers appeared slightly swollen and stiff. There were signs of a minimal effusion on the right side of the chest. The spleen and liver were not palpable.

Investigations.

Skiagrams.—Extensive hilar gland calcification with pleural thickening at both bases, extending into the fissures.
Barium swallow.—Normal.
Hands.—Normal.
E.C.G.—Normal.
Blood count.—Hb 9·6 g./100 ml. W.B.C. 5000 (Neutros. 68%).
E.S.R.—55 mm/hr.
Urine.—Moderate proteinuria.
Lupus erythematosus cells were prepared from peripheral blood.

The patient was treated with oral prednisone 60 mg. daily and the fever settled in four days, with general improvement. After one month the skin lesions had cleared and her general improvement was maintained. The prednisone was gradually reduced to a maintenance dose of 15 mg. daily and by the end of the third month she was well enough to be transferred to a convalescent hospital. From there she went home at the end of the fourth month, to continue a maintenance dose of 15 mg. daily.

Two months after admission, urinary protein excretion was normal and simple renal function tests were normal. Blood urea was 34 mg. per 100 ml. Plasma electrolytes were normal. The E.S.R. had fallen to 11. A urinary cell count (Dr. B. J. Houghton) showed slightly raised cell excretion.

In view of the latter finding it was decided to proceed with a percutaneous needle biopsy of the kidney and this was performed on 12.ii.57. The small piece of kidney was fixed in " corrosive-acetic " (90 ml. saturated mercuric chloride and 10 ml. glacial acetic acid) and sections 5 μ thick were cut serially and all mounted, six per slide. Most slides were stained with haematoxylin and eosin ; other stains used were haematoxylin and van Gieson's mixture, periodic acid-Schiff and methyl violet.

Twenty-four glomeruli were present and of these six were abnormal. The most conspicuous change was one which occurred at the periphery of the capillary tuft, often affecting a single lobule. It consisted of proliferation of cells with deeply staining nuclei, the affected area sometimes having a rounded appearance (Fig. 1). The adjacent epithelium lining Bowman's capsule usually showed proliferation, and adhesions between this and the tuft were frequent. In some of the glomerular lesions small foci of eosinophilic staining material were seen, but these were never extensive and appeared to begin in or near the basement membrane (Fig. 2). Pyknotic nuclear remnants were sometimes seen in the proliferative foci and occasionally small areas of diffuse purple material were present. Apart from mild intimal thickening of interlobular arteries there were no other remarkable abnormalities.

Discussion.

The presence of a typical skin lesion for many years with no evidence of generalized systemic involvement suggests that the acute febrile episode associated with the positive L.E. cell phenomenon represented the acute onset of systemic lupus erythematosus. Rapid response to prednisone without any other form of therapy is strongly in favour of the diagnosis. The only clinical evidence of renal involvement was the presence of proteinuria during the febrile episode, and shortly before the renal biopsy a moderate increase in the urinary cell excretion.

In discussing the renal lesion of systemic lupus erythematosus, Klemperer *et al.*, described areas of focal necrosis occurring at the periphery of glomerular

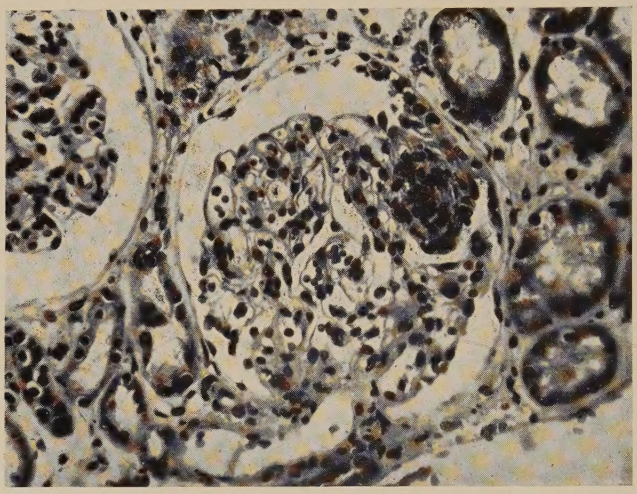

FIG. 1.—Circular area of cellular proliferation affecting periphery of a lobule. There is some proliferation of epithelium lining Bowman's capsule. H. & E. × 250.

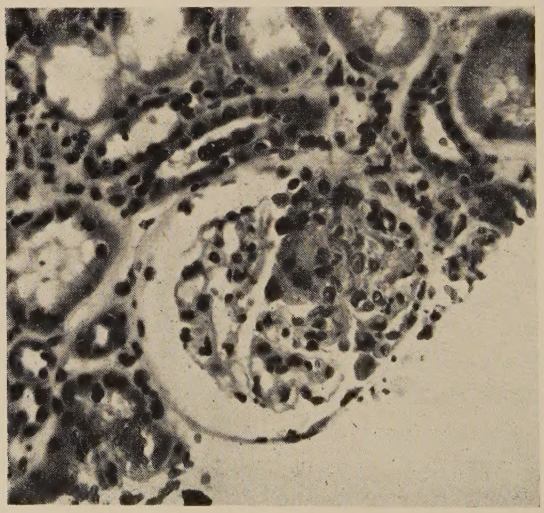

FIG. 2.—Glomerulus with lesion at periphery showing focal necrosis. H. & E. × 250.

tufts and their Fig. 7A could quite well come from the case under discussion. While putting more emphasis on the " wire loop " lesion they mentioned that in 5 of their cases, focal necrosis of the tuft occurred in the absence of " wire loops ". Smith (1955) called particular attention to the focal necrosis of the glomeruli and considered that the fundamental lesions were the presence of haematoxyphil bodies and of hyaline protein material. Muehrcke, Kark, Pirani and Pollak (1957) believed local glomerular necrosis to be almost pathognomonic of systemic lupus erythematosus and found the change in 13 out of 40 biopsies. Haematoxyphil bodies however were found in only 4 of these. In the present case the local glomerular proliferation was the most remarkable feature, occurring with or without eosinophilic areas, which were interpreted as being foci of necrosis. No unequivocal haematoxyphil bodies, of the kind considered by Klemperer *et al.* (1950) to be depolymerized ribose-nucleic acid derived from cell nuclei, were seen in the present case, although the diffuse purplish areas occasionally seen might have been of this nature. " Wire loops " were completely absent and no conspicuous basement membrane changes were present.

It is very probable that the renal involvement in the present case dated from the acute systemic episode three months before the biopsy. The predominant renal lesion was a cellular proliferation affecting only a part of a glomerulus, with the majority of the glomeruli remaining unaffected. Where necrosis was present in the localized lesions, it was less obvious than the cellular proliferation. This is in marked contrast to the glomerular lesion of polyarteritis nodosa of the so-called microscopic type (Davson, Ball and Platt, 1948) where necrosis is the dominant feature.

Summary.

The histology of renal changes in a case of systemic lupus erythematosus is described, kidney tissue being obtained by percutaneous needle biopsy.

Renal involvement in this case was probably only of three months' duration.

The predominant lesion consisted of a cellular proliferation, with or without necrosis, affecting only part of the periphery of a minority of the glomeruli.

We are grateful to Dr. G. B. Mitchell-Heggs for permission to publish this case.

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THE IMMUNOLOGICAL ASPECT OF SARCOIDOSIS.

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The immunological responses of patients with sarcoidosis usually differ in certain important ways from those of healthy subjects. These immunological anomalies are interesting because they form the basis of certain skin tests used as an aid to the diagnosis of sarcoidosis, and also because they provide evidence about possible causes of the disease.

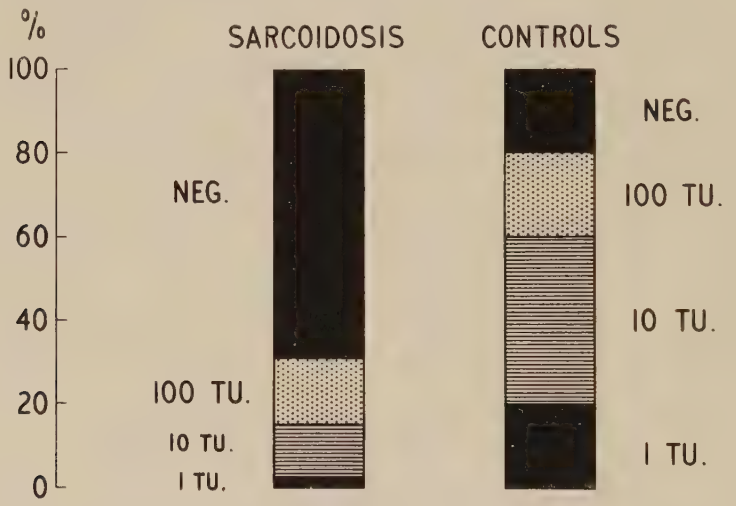

Fig. 1.—Tuberculin sensitivities of 102 patients with sarcoidosis and 35 control subjects.

The purpose of this paper is to review recent knowledge of the immunological aspect of sarcoidosis and to discuss the evidence which this provides about the relationship between sarcoidosis and tuberculosis.

The Reaction of the Skin to Tuberculin.

The best known immunological feature of sarcoidosis is the frequency with which patients suffering from the disease fail to react to tuberculin. The extent and significance of insensitivity to tuberculin in sarcoidosis has been the subject of controversy and speculation.

The tuberculin sensitivities of 102 patients with histologically confirmed sarcoidosis are shown in Fig. 1. These results are compared with the tuberculin sensitivities of 35 control patients of similar age and sex distribution derived

from the same geographical area (Citron, 1957). About 70% of the sarcoidosis patients failed to react to 100 t.u. of P.P.D. compared with 20% of the controls. Twenty per cent. of the controls were highly tuberculin sensitive, reacting to 1 t.u. in contrast to only 2% of the sarcoidosis patients reacting to this dose. Low tuberculin sensitivity may, therefore, be regarded as a characteristic of sarcoidosis.

The Reaction of the Skin to Other Antigens.

This insensitivity to tuberculin is not an isolated finding in sarcoidosis, but is a reflection of a general deficiency of skin reactions of the delayed type.

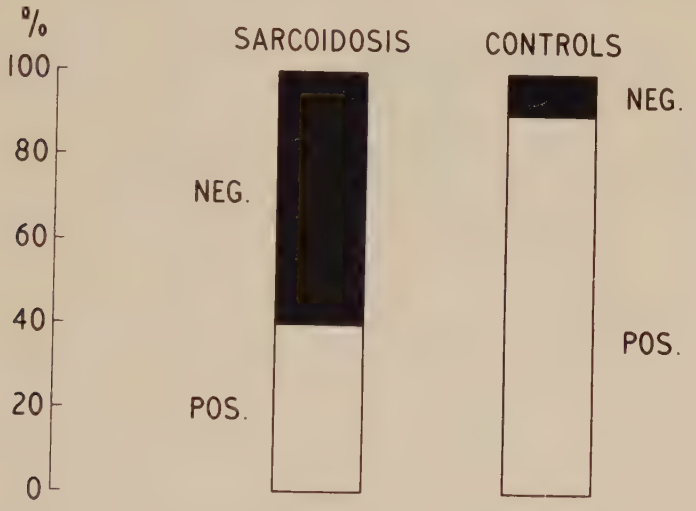

FIG. 2.—*Candida albicans* antigen skin sensitivity of 30 patients with sarcoidosis and 60 control subjects.

Poverty of response has been reported to several other antigens which usually elicit a delayed response, including trichophytin, mumps virus and pertussis agglutinogen (Sones and Israel, 1954). The results of a survey of sensitivity to *Candida albicans* antigen, a yeast antigen eliciting delayed tuberculin-type responses (Citron, 1957), are shown in Fig. 2. The responses of 30 sarcoidosis patients are compared with those of 60 controls of similar age composition; 90% of control patients reacted compared with only 40% of sarcoidosis patients. Fig. 3 shows both tuberculin and *Candida* sensitivity and shows a striking difference between the sarcoidosis and control patients, for whereas 84% of controls reacted to both antigens only 7% of the sarcoidosis patients did. Only 2% of the control patients failed to react to both antigens whereas 43% of sarcoid patients gave negative reactions to both.

In contrast to the poverty of reactions of delayed type, skin reactions of

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immediate type, or histamine release reactions, are normal in sarcoidosis ; and circulating antibodies develop normally in response to antigens producing immediate-type reactions (Israel and Sones, 1955). Thus sarcoidosis patients may suffer from urticaria, angioneurotic oedema or allergic asthma.

Causes of Deficiency of Delayed-type Skin Responses in Sarcoidosis.

What is the cause of the lack of delayed-type immunological response? In discussing this question, I will take the tuberculin reaction as my example since this test has received the most study.

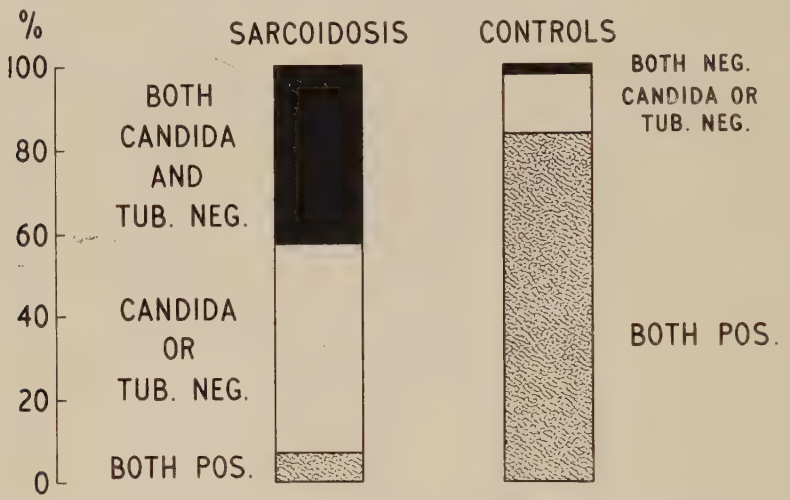

Fig. 3.—Sensitivity to tuberculin and *Candida albicans* in sarcoidosis and controls.

The principal factors upon which the tuberculin reaction in the skin is dependent are :

(i) The capacity of the skin to react to the inflammatory stimulus resulting from the antibody-antigen reaction.

(ii) The local persistence of the antigen (tuberculin) in the skin.

(iii) The concentration of antibody in the skin.

The capacity of the skin to react to inflammatory stimuli in sarcoidosis is normal. This has been shown by cellular transfer of tuberculin sensitivity to patients with sarcoidosis : If leucocytes from a tuberculin-positive donor are injected into the skin of a tuberculin-negative sarcoid patient, and the area is challenged with tuberculin, a positive tuberculin response occurs (Urbach, Sones and Israel, 1952). The occurrence of a normal tuberculin reaction by cellular transfer also demonstrates that the antigen, tuberculin, must be normally fixed in the skin of sarcoidosis patients.

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The failure to react seems therefore to be due to deficiency of the antibody in the skin. Tuberculin antibody cannot be demonstrated as free circulating antibody in plasma. Tissue culture experiments indicate that it is not present in the dermis either (Cruickshank, 1951). There is good evidence that tuberculin antibodies are produced and transported by cells of reticulo-endothelial system and that the antibody is brought to the site of challenge in the skin by cells, principally lymphocytes, which migrate into the site (Pepys, 1955). This accounts for the delayed nature of the tuberculin reaction. The various possibilities which can be envisaged for deficiency of cellular tuberculin antibodies in the skin are :—

(i) Lack of transporting cells.

(ii) Tuberculin neutralizing antibodies, " anticutins ".

(iii) Depressed production of antibodies by the reticulo-endothelial system.

Depression of circulating leucocytes especially lymphocytes is known to depress tuberculin sensitivity, but there is no deficiency of circulating white cells in sarcoidosis.

In regard to anticutins, several workers (Pickert and Lowenstein, 1908 ; Wells and Wyllie, 1949 ; Sterling, 1950) have noted that if a dose of tuberculin sufficient to elicit a reaction in a tuberculin-positive donor is mixed with serum from a sarcoidosis patient before injection it may then fail to give a reaction on injection of the mixture into a tuberculin-sensitive subject. This has been held by some to indicate the presence in sarcoidosis serum of a tuberculin neutralizing antibody or " anticutin ". The useful work of Magnusson (1956), however, suggests that the explanation is much simpler than this. He found that a proportion of tuberculin-sensitive recipients failed to react to tuberculin when it was injected mixed not only with sarcoidosis serum but sometimes also with serum from persons without sarcoidosis.

Inhibition took place only in those reactions where a wheal appeared 15 minutes or so after the injection of the serum-tuberculin mixture. This wheal probably caused washing away of the tuberculin, for it has been clearly demonstrated that whealing agents reduce or abolish tuberculin reactions non-specifically by preventing fixation of the antigen tuberculin at the site of injection (Pepys, 1955). This, together with other evidence, makes it unlikely that tuberculin neutralizing antibodies are present in sarcoidosis.

Diminished production of antibody seems to be the likely cause of deficiency of antibody in sarcoidosis. Passive transfer of leucocytes from sarcoidosis patients to tuberculin-negative recipients (Urbach, Sones and Israel, 1952) and tests of tuberculin sensitivity of sarcoidosis leucocytes in tissue culture (Citron, 1957*b*) indicate that in sarcoidosis tuberculin antibody is deficient.

Latent Tuberculin Sensitivity and the Tuberculin-cortisone Skin Test.

Recent work indicates that there is a deficiency rather than complete absence of tuberculin antibody in sarcoidosis. This was suggested by the observation by Pyke and Scadding (1952) that patients with sarcoidosis who were insensitive to tuberculin might, under the influence of local or systemic cortisone, react to tuberculin. Citron and Scadding (1957) have investigated further the effect of cortisone acetate injected with the tuberculin used for the Mantoux test.

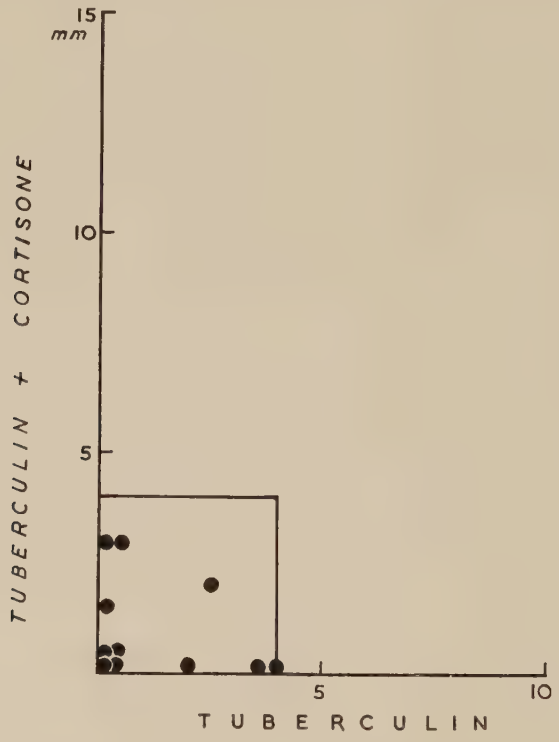

Fig. 4.—Reactions (4 mm. of induration) to 100 t.u. of tuberculin and to the same dose of tuberculin + cortisone, in 11 healthy tuberculin-insensitive subjects.

Fig. 4 shows the results in healthy tuberculin-insensitive subjects. In this diagram the skin reaction to 100 tuberculin units (t.u.) of tuberculin and also the reaction to 100 t.u. tuberculin mixed with 1·25 mg. of cortisone acetate is shown for each subject. No appreciable reaction occurs in response to tuberculin + cortisone in these healthy tuberculin-negative subjects. Fig. 5 shows the effect of the test in tuberculous patients who had been desensitized to tuberculin by the intramuscular injection of increasing doses of tuberculin until the skin failed to react to 100 t.u. It is seen that 70% of these patients gave an appreciable response to the injection of tuberculin with cortisone in contrast to

the absence of response in the control group mentioned previously. This evidence suggests that the addition of cortisone to the tuberculin in some way enables the detection of a degree of tuberculin sensitivity too slight to be detected by tuberculin alone.

Fig. 6 shows the results of the same test in sarcoidosis patients who failed to react to 100 t.u. or more of tuberculin. It will be seen that 50% responded to tuberculin with cortisone. This suggested that latent tuberculin sensitivity occurred in half these apparently tuberculin-insensitive sarcoidosis patients.

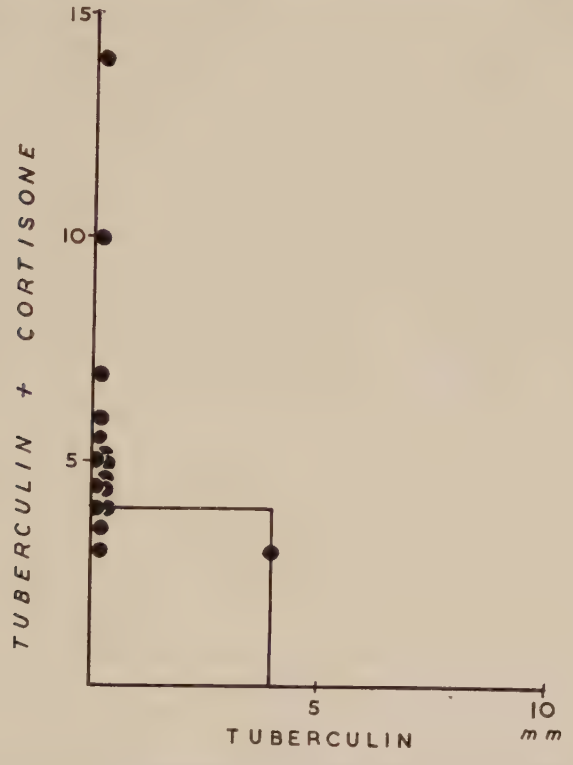

Fig. 5.—Reactions to 100 t.u. of tuberculin, and to the same dose of tuberculin + cortisone, in 16 patients with pulmonary tuberculosis who had been desensitized to tuberculin.

Similar evidence of prevalence of tuberculin sensitivity of low degree in a high proportion of apparently tuberculin-insensitive sarcoidosis patients has been afforded by the use of oily " depot " tuberculin (James and Pepys, 1956).

What is the cause of this poor production of antibodies?

It has been suggested that the peculiar granulomatous reaction in sarcoidosis results in the destruction of tubercle bacilli within the body and also prevents re-infection so that tuberculin sensitivity wanes. However, study of B.C.G. lesions in sarcoidosis does not support this, for although tuberculin sensitivity often fails to develop or if developed is transient after B.C.G. inoculation in

sarcoidosis, the B.C.G. organisms are killed off no more rapidly in sarcoidosis patients than in controls (Rostenberg *et al.*, 1953).

It is interesting to note that a similar deficiency of delayed type reactions has been noted to occur in Hodgkin's disease (Schier *et al.*, 1956). It has been suggested that the immunological anomalies in both sarcoidosis and Hodgkin's disease are related to the localization of both diseases in the reticulo-endothelial system rather than to the actual nature of the disease processes.

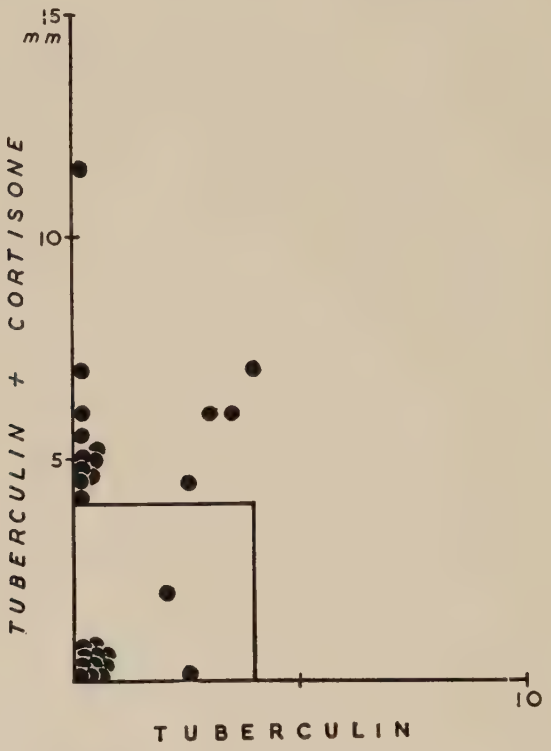

Fig. 6.—Reactions to tuberculin and to tuberculin + cortisone in 28 patients with sarcoidosis who did not react to tuberculin alone.

The Kveim Test.

The intradermal injection of a suspension of sarcoid tissue in patients suffering from sarcoidosis may stimulate the production of a nodule at the site in about 4–6 weeks. The histological appearance of this nodule may be indistinguishable from sarcoidosis. This forms the basis of the Kveim test for sarcoidosis (Kveim, 1941).

To be of diagnostic value the test must satisfy two criteria :

(1) It must not produce sarcoid-like lesions in conditions other than sarcoidosis,

(2) It must produce specific lesions in a sufficient proportion of cases of sarcoidosis.

Published work on the Kveim test indicates that these criteria are not always fulfilled.

Thus although James and Thomson (1955) found no false positives, Israel and Sones (1955) found 42% false positives in tuberculosis. Again Siltzbach and Ehrlich (1954) found 86% positives in sarcoidosis but Israel and Sones (1955) only 21%. Such variability seems to be due to inconsistences of the antigen. I believe that the diagnostic value of the Kveim test cannot be relied upon unless the antigen has been assayed and found satisfactory in a sufficient number of sarcoidosis patients and controls.

The Kveim test is of great interest in relation to the aetiology of sarcoidosis. The test material consists of a suspension of sarcoid tissue. Of particular significance therefore is the claim to have isolated from sarcoid tissue diaminopiomelic acid and mycolic acid (Nethercott and Strawbridge, 1956) which are known to occur in mycobacteria but are said not to occur in normal human tissue. Could the Kveim response be a tissue reaction to these bacterial residues of mycobacteria present in the antigen? The suggestion is strengthened by the finding that tubercule bacilli dead or alive, B.C.G. or lipo-polysaccharide of mycobacteria may stimulate sarcoid reactions in sarcoidosis.

The Relationship between Tuberculosis and Sarcoidosis.

These considerations bring me to the question of the relationship between tuberculosis and sarcoidosis. The use of the tuberculin-cortisone test for the detection of low degrees of tuberculin sensitivity has thrown some light on this. The results of the investigation (Citron and Scadding, 1957) of 49 patients with sarcoidosis using this test are shown in Fig. 7.

Forty-two per cent. of the patients reacted to tuberculin alone and another 29% failed to react to tuberculin alone but reacted to tuberculin + cortisone. The remaining 29% failed to react both to tuberculin alone and to tuberculin + cortisone. If the proportion (29%) is compared with the 20% of the controls insensitive to tuberculin it suggests that the proportion not infected by tuberculosis was similar in the control and sarcoidosis groups. It might be thought therefore that sarcoidosis merely depressed tuberculin sensitivity already acquired from previous tuberculous infection. However further investigation provided another explanation.

The proportion of sarcoidosis patients in whom there was radiological or bacteriological evidence of previous tuberculous infection probably contracted before the onset of the sarcoidosis was analysed. This is shown by the dotted sections in the diagram. It is seen that the proportion with evidence of previous tuberculous infection was the same in the tuberculin-insensitive group as in the

groups sensitive either by the tuberculin test or the more sensitive tuberculin + cortisone test. This finding is entirely compatible with the view that sarcoidosis is a manifestation of tuberculous infection in which depressed tuberculin sensitivity is a feature of the peculiar tissue reactivity which determines the development of sarcoidosis. This observation adds to the growing evidence that there is a causal relationship between tuberculosis and sarcoidosis. The reason why these patients react to tuberculous infection by this unusual histological and immunological response instead of by the usual caseating tuberculin

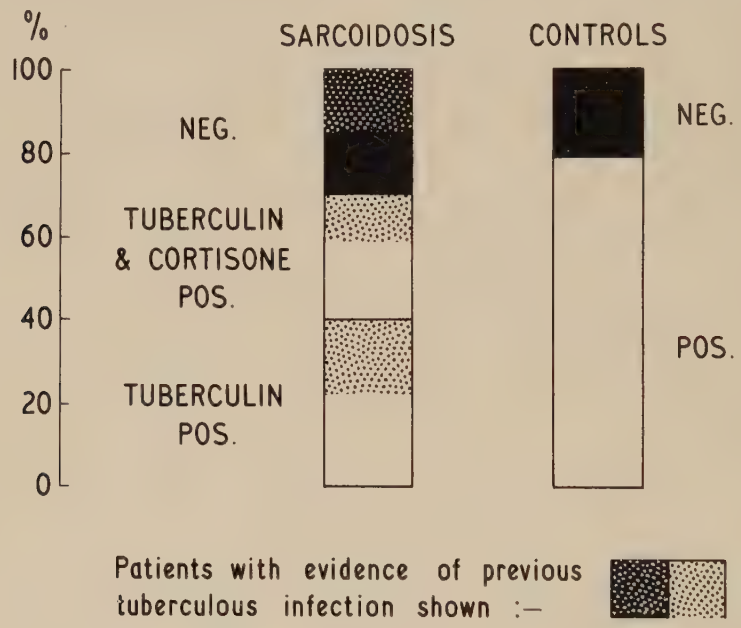

Fig. 7.—The sensitivity of 49 patients with sarcoidosis to tuberculin alone and to tuberculin + cortisone and the proportion of these patients with evidence of previous tuberculous infection.

positive reaction remains an unsolved and challenging problem. Indeed, there are many problems in sarcoidosis which remain unsolved, the ultimate elucidation of which will not only throw light upon this disease, but will clarify fundamentally our understanding of the basic mechanisms of the immunological response of the body in health and disease.

Summary.

Investigations using tuberculin and other antigens have shown that in sarcoidosis there is a lack of skin reaction of the delayed type, in contrast to normal skin reactions of the immediate type.

The use of tuberculin with cortisone and tuberculin in oil has revealed the

presence of latent tuberculin sensitivity of slight degree in a high proportion of sarcoidosis patients.

Possible causes of these immunological anomalies are reviewed and evidence is presented which indicates that it is due to a relative deficiency in the production of delayed-type antibodies. The Kveim test is discussed in relationship to the diagnosis and aetiology of sarcoidosis.

An immunological survey in sarcoidosis is described which has provided evidence suggesting that sarcoidosis may result from tuberculous infection.

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I am indebted to the Editor of the *Quarterly Journal of Medicine* for permission to reproduce Figs. 4, 5 and 6.

STEROID THERAPY IN RETICULOSIS OF THE SKIN WITH SPECIAL REFERENCE TO EXFOLIATIVE DERMATITIS.

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Simple symptomatic exfoliative states may respond dramatically to treatment with steroids and reticulosis as manifested in acute lymphoblastic leukaemia may show temporary regression with such therapy. Reticulosis of the skin, which often presents as exfoliative dermatitis, might accordingly be expected to show response to the administration of adrenocortical hormones.

Temporary diminution of pruritus and improvement in the skin have been noted in occasional cases of mycosis fungoides by Tulipan (1950), Taylor *et al.* (1950), Schuppli (1951), Costello (1951), Steiner and Frank (1952), Hopkins *et al.* (1952), Miescher (1952), Kierland *et al.* (1952) and others. Ingram (1956) found that pruritus and infiltration were diminished in some cases, but Lever (1951), Goldsmith and Hellier (1954) and Degos (1955) considered that steroids are of little value in the management of mycosis fungoides. The histological appearances in the premycotic stage of this disease may be such that the diagnosis rests upon opinion short of proof, and the natural course of this singular eruption makes it difficult to assess the response to treatment. Bearing these considerations in mind, we present the results of steroid treatment in ten patients in whom the diagnosis of early mycosis fungoides appeared probable on clinical and histological grounds, and in one patient who was suffering from reticulosarcoma. Clinical and histological details are given in Tables I and II.

Comment.

The quantity and quality of the cellular infiltrate together with the pleomorphism and nuclear changes evident in the sections warrant a presumptive diagnosis of malignant reticulosis of the skin. Cases 7 and 9 at first showed simple non-specific histological appearances and we believe that with prolonged observation so-called idiopathic exfoliative dermatitis and perhaps pityriasis rubra of Hebra often develop features of reticulosis.

Natural remissions and relapses which may occur are illustrated by Case 6, and doubt regarding the part played by treatment may be raised also in Case 5.

This difficulty does not arise in the other patients. The duration of the eruption prior to steroid treatment, the lack of response to other methods of therapy, the immediate improvement on administration of the hormones and the ready tendency to relapse on reduction of dosage all indicate that clinical improvement was directly related to steroid therapy. Although it is usually not difficult to decide whether treatment should be continued indefinitely, the problem arises in Cases 3, 4 and 6 where the patients are almost completely free from signs and symptoms but where some evidence of a continuing pathological process remains. No final answer can be given until such patients have been under observation for a long period, but at least we have noted no exacerbation following cessation of therapy. In our experience treatment with ACTH remains superior to prednisone. The ease of administration of cortisone and prednisone can be dangerous in out-patients and they are apparently less effective in some subjects. Prednisone is not devoid of toxic effects ; diastolic hypertension may occur with moderate doses and moon-face, acne, infections and hypokalaemia may appear when daily maintenance doses are above 15 mg.

It is interesting to note that during treatment with corticotropin in Case 8 the tumours regressed rapidly while at the same time *Trichophyton rubrum* infection spread quickly over the trunk. A fungus (*Candida tropicalis*) was also cultured from the feet in Case 11. Lewis *et al.* (1953) observed that in three patients a generalized *Trichophyton rubrum* infection was associated with systemic lymphoblastoma and a possible relationship between fungus and lymphoma has been suggested by many. Such coincidences are perhaps more likely to be fortuitous, or they may occur because a ubiquitous fungus finds a suitable medium in disordered skin.

We believe that steroids are the treatment of choice in premycotic exfoliative states and that they have a place in the management of the tumour phase of the disease and also of "*tumeurs d'emblée*" or reticulosarcoma of skin. In these closely related conditions, x-ray therapy ("shower bath" and focal), urethane or nitrogen mustard may indeed produce temporary improvement (perhaps mediated in part through the adrenal cortex), but there may be subsequent severe exacerbations of the disease process, the natural course of which may also sometimes be shortened by adverse effects on haemopoiesis. There can be no doubt that steroids may produce a remarkable and beneficial effect in exfoliative states even when histological findings are suggestive of early mycosis fungoides. How those hormones act remains uncertain, for it is debatable whether effects such as lymphocytolysis and lymphopenia are sufficient in themselves to account for the regression of skin pathology. Anti-anabolic properties of corticosteroids may conceivably suppress tumour growth, but if such suppression occurs then our experience indicates that tumour cells may become refractory to hormonal inhibition. Neoplastic processes finally free themselves from physiological bonds and we are inclined

Table I

Case No.	Age and sex.	Disease state.	Duration of eruption (years).	Duration of treatment (days).	Result.
1	75 M.	Pityriasis rubra pilaris Exfoliative dermatitis Silicosis	5	49	Skin greatly improved. Marked oedema developed. Died.
2	69 F.	Exfoliative dermatitis Infiltrated plaques Oedema of legs	1	10 None 83	Cleared completely. No oedema. Recurred. Cleared, then developed widespread pustular eruption, diabetic blood sugar curve and large abscess. These complications cleared up and skin remained almost well for more than one year. Patient died of cerebral haemorrhage.
3	59 M.	Exfoliative dermatitis Oedema of legs and sacral region Enlarged axillary and inguinal glands	1	1190	Cleared completely. No oedema. Developed erysipelas, generalized herpetiform eruption and finally a severe urticarial reaction to a new brand of ACTH. Now well apart from a few pruritic nodules on legs, 340 days after treatment discontinued.
4	66 F.	Parapsoriasis en plaques Premycotic change	6	43	Cleared completely. Parapsoriasis recurred after stopping treatment and still present 4 years later.
5	44 M.	Exfoliative dermatitis Oedema of feet and sacral region Enlarged axillary and inguinal glands Enlarged liver and spleen	5/52	34	Skin well but pigmented. No oedema. Reported to be well 4 years later.
6	55 F.	Exfoliative dermatitis Oedema of legs and sacral region Enlarged axillary and inguinal glands	14/365	84 None	Skin greatly improved after 7 days and then cleared completely. No oedema. Recurrence 41 days later. Cleared completely in 41 days with local treatment only. Recurrence 55 days later and cleared completely in 65 days with local treatment only. Remains well apart from occasional urticarial papules more than 2 years later.

TABLE I—*continued.*

Case No.	Age and sex.	Disease state.	Duration of eruption (years).	Duration of treatment (days).	Result.
7	54 M.	Exfoliative dermatitis Enlarged axillary and inguinal glands	3/12	56	Improvement after 12 days, but not maintained on 200 mg. ACTH daily.
		Pernicious anaemia		None	Relapse.
				365	Skin cleared completely on 240 mg. ACTH gel. daily and remained well on 40 mg. ACTH gel + 50 mg. cortisone daily. Made good recovery from lobar pneumonia, abscess and thrombo-phlebitis during steroid therapy. Finally developed increasing fatigue and breathlessness and died. ? coronary thrombosis. No P.M.
8	46 M.	Gyrate plaques	13	694 and continuing	Pruritus ceased after 3 days and tumours regressed after 4 days. Remained well for some months then gradual recurrence on 30 mg. ACTH gel daily.
		Tumours	3/12		Controlled again on 20 mg. ACTH gel + 20 mg. prednisone daily. Pruritus and tumours now recurring again. *Trichophyton rubrum* cultured from scaling lesions on trunk.
9	53 M.	Exfoliative dermatitis Oedema of legs Enlargement of axillary and inguinal glands	1/12	450 and continuing	Skin well. Made good recovery from lobar pneumonia during steroid therapy. No oedema. Maintained on 15 mg. prednisone daily.
10	59 M.	Exfoliative dermatitis Oedema of legs	8/12	296	Skin well. Some increase in diastolic B.P. Maintained on 7·5 mg. prednisone daily. No oedema. Gradual recurrence of oedema and slight relapse of skin condition. Prednisone increased to 12·5 mg. daily. Patient died. ? coronary thrombosis. No P.M.
11	71 M.	Exfoliative dermatitis Gross oedema of legs and lower trunk Enlarged inguinal glands	1	197 and continuing	Skin greatly improved within a few days and then cleared completely. Made good recovery from bronchopneumonia. Oedema gradually regressed. *Candida tropicalis* cultured from feet. Maintained on 20 mg. ACTH gel daily.

TABLE II—*Histological Appearances.*

Case no.	Date.	
1	27 : xi : 52	Marked acanthosis and oedema of epidermis. Considerable infiltrate in the upper corium consisting of cells resembling lymphoblasts, lymphocytes, reticulum cells and eosinophils—strongly suggestive of a lymphoblastoma.
	12 : xii : 52	Epidermal changes compatible with pityriasis rubra pilaris. The changes in the corium as in previous section.
	31 : xii : 52	ACTH started.
2	24 : vii : 52	The epidermis is moderately acanthotic with areas of localized intracellular oedema and superficial crusting. The corium is oedematous and there is a moderate perivascular infiltrate of mononuclear cells of varying size and eosinophils—possible premycotic eruption.
	3 : xi : 52	The infiltrate in the corium is rather pleomorphic and contains numerous pycnotic and distorted nuclei—highly suspicious of early mycosis fungoides.
	22 : i : 53	The infiltrate has increased in amount and is more pleomorphic—early mycosis fungoides.
	4 : ii : 53	ACTH started.
	19 : iii : 53	Recent patchy fibrosis and the formation of new capillaries. A few foci of chronic inflammatory cells are seen in the upper corium; no evidence of mycosis fungoides.
3	27 : xi : 52	Subacute eczema. The quality of the infiltrate with numerous pycnotic nuclei suggests a premycotic change.
	27 : ii : 53	Extensive serous crusting and patchy parakeratosis. The epidermis is markedly acanthotic and rather oedematous. A dense pleomorphic cellular infiltrate is present in the upper corium, with numerous mitotic figures and pycnotic nuclei—mycosis fungoides.
	27 : ii : 53	ACTH started.
	6 : i : 54	In the corium are nodules, rather closely related to small vessels and showing considerable variation of cell type with some large cells of reticulum type. Mitoses are very few and the lesions are much better circumscribed and less active than in the previous biopsy, but the process is basically the same and still active though in a reduced degree.
	31 : v : 56	ACTH stopped.
	7 : vi : 56	Nodule from left knee—mycosis fungoides.
4	8 : i : 51	Right scapular region: Mild oedema of the epidermis with a slight non-specific chronic inflammatory infiltration in the upper corium—consistent with parapsoriasis. Lumbar region: Moderate acanthosis and oedema of the epidermis. Below this is an area of rather pleomorphic cellular infiltration in which an occasional mitotic figure is seen. Several of the cells have shrunken pycnotic nuclei—suspicious of a premycotic change.
	16 : iii : 53	Consistent with parapsoriasis. No evidence of premycotic change.
	18 : iii : 53	ACTH started.
	8 : ii : 54	Marked oedema of epidermis. Small collections of mononuclears in epidermis. Dermal infiltrate pleomorphic with pycnotic nuclei. Early mycosis fungoides.
5	4 : iii : 53	Considerable parakeratosis with oedema and acanthosis of the epidermis. The upper corium is oedematous and there is a patchy cellular infiltrate around the blood vessels and dermal appendages. This infiltrate is rather pleomorphic and contains many eosinophils and pycnotic nuclei—highly suspicious of early mycotic change.
	21 : iii : 53	ACTH started.
	27 : iv : 53	Mild non-specific eczematous process.

TABLE II—*continued.*

Case no.	Date.	
6	3 : xi : 53	Lymph node—lipomelanic adenopathy.
	2 : xii : 53	Marked cellular infiltration extending down to the subcutaneous fat strongly suggesting early mycosis fungoides.
	14 : xii : 53	ACTH started.
	13 : i : 54	The cellular exudate is much less and extends less deeply ; it is still markedly perivascular. Pycnotic cells are numerous. In the upper layers of the corium early post-inflammatory fibrosis is seen and a little iron pigment marks the site of the previous infiltration. The lesion seems inactive if not extinct.
	27 : i : 54	The epidermis is normal apart from an increase in melanin in the basal layer. A few foci of perivascular infiltrate are seen in the corium. Not recognizable as mycosis fungoides.
	29 : iv : 54	Strongly suggestive of early mycosis fungoides.
7	19 : xii : 53	Non-specific exfoliative dermatitis.
	7 : i : 54	ACTH started.
	15 : ii : 54	Non-specific subacute eczema.
	19 : v : 54	Infiltrate highly suspicious of premycotic change. Small Pautrier-type microabscesses.
8	23 : vi : 51	There is patchy parakeratosis. The epidermis is acanthotic and oedematous. There are numerous mononuclear microabscesses and considerable infiltration of the epidermis by polymorphonuclear leucocytes. The upper corium is oedematous and infiltrated by inflammatory cells exhibiting pleomorphism and nuclear pycnosis. These cells extend downwards into the deep corium as a mantle around the blood vessels—early mycosis fungoides.
	28 : ix : 55	Dense cellular infiltrate involving the entire cutis—reticulosarcoma. No fungus in stained section.
	11 : x : 55	ACTH started.
	26 : x : 55	Evidence of regression with decrease in cellularity and also considerable nuclear pycnosis. No fungus in stained section.
	27 : x : 55	Patchy epidermal oedema with parakeratosis. A perivascular infiltrate, predominantly lymphocytic, is present in the upper corium. No fungus in stained section.
9	30 : iii : 56	Subacute eczema ; no evidence of reticulosis.
	23 : v : 56	Lymph node—lipomelanic adenopathy.
	7 : vi : 56	Marked acanthosis with oedema and patchy parakeratosis. There is a rather pleomorphic infiltrate in the dermis in which plasma cells are prominent. A few pycnotic nuclei are seen—suggestive of an early premycotic change.
	11 : vi : 56	Prednisone started.
10	17 : viii : 56	Acanthosis and oedema of the epidermis with marked parakeratosis. The corium is oedematous and there is considerable perivascular infiltrate of rather pleomorphic character and showing a tendency to nuclear pycnosis—suggestive of early mycosis fungoides.
	6 : ix : 56	Prednisone started.
11	19 : ii : 57	ACTH started.
	21 : ii : 57	Irregular acanthosis and oedema of epidermis with marked parakeratosis. The corium is oedematous and there is a considerable pleomorphic cellular infiltrate with reticulum cells, histiocytes, lymphocytes and an occasional eosinophil. There is considerable nuclear pycnosis—strongly suggestive of a premycotic eruption.

to believe that in bringing about the regression of premycotic exfoliative states the anti-inflammatory effect of steroids is likely to be more important than any possible anti-anabolic action. The disappearance of oedema in the present series of cases was an early and evident sign of this response. In eczematous and exfoliative states. if they result from reticulum-cell activity, hormones with anti-inflammatory properties may be expected to produce symptomatic relief; but if eczema and exfoliative dermatitis themselves produce reticulosis of the skin, prevention of the latter may be within the bounds of possibility.

Summary.

The results of steroid therapy in ten cases of premycotic exfoliative dermatitis and in one case of reticulosarcoma of skin are described and discussed.

Treatment was maintained for periods varying from 34 to 1190 days. It is suggested that this is the treatment of choice in premycotic exfoliative states and that it may have a place in the management of reticulosarcoma of the skin.

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WEST OF ENGLAND AND WALES DERMATOLOGICAL SOCIETY.

Exeter, May 1957.

Cases shown by Dr. J. R. Simpson.

Eosinophilic Granuloma of Skin.

A boy aged 17 months.

At the age of 2 months a papule appeared on the left forearm and one on the thigh, which grew rapidly and ulcerated. These were followed by several others.

When first seen (May, 1956), he was well developed and in good general condition. There were twelve skin nodules situated on face, scalp, thighs, sacral region, left arm, right wrist and right heel. The early lesions were pale yellow and glistening and later became orange in colour. The two largest were ulcerated and dark red; that on the left arm measured 2·3 × 1·2 cm. and that on the left thigh 2·5 × 1·8 cm. The rest of the skin was normal. General examination was normal.

Histology.—There is a compact cellular infiltration throughout the dermis, most dense in the papillary layer, consisting of eosinophils and endothelioid cells; the latter do not contain lipoid stainable by Sudan III.

Skiagrams.—Entire skeleton and chest—normal.

Serum cholesterol 187 mg.%. Blood count—normal (eosinophils 400).

Progress.—All lesions were treated with x-ray (130 kV., total dose 3000–3500 r in 16–40 days). All the nodules increased in size until treated and then regressed rapidly within a month of treatment; they became hard and many have turned a bright yellow colour. Further biopsy was refused. The lesion over the sacrum was excised and has not recurred.

The child's general condition and development has been normal.

Sarcoidosis.

A man aged 37.

A lesion appeared on the right cheek in 1947, and was followed by others during the next five years. There were no other symptoms.

He was first seen on 13 : x : 52 and then had red indurated lesions on the cheeks, pinna, neck, back and all limbs. A lesion on the right shin was ulcerated and somewhat resembled necrobiosis lipoidica.

Investigations.—Mantoux 1 : 1000—negative. E.S.R.—4 mm/hr. W. R. and Kahn —negative.

Skiagrams.—Hands and feet—normal; chest—"Changes in both mid-zones suggesting probability of sarcoidosis or tuberculosis".

Histology.—(Lesion on arm) typical changes of sarcoidosis. (Lesion on right shin, June 1957) typical sarcoidosis.

Treatment.—Calciferol 100,000 units daily for 12 months; well tolerated but very little improvement. Prednisone 20 mg. daily for last seven weeks; considerable improvement.

The following cases also were shown:

Multiple Basal Cell Epithelioma; Incontinentia Pigmenti; Sebaceous Hypertrophy; Dermatomyositis.

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY

Liverpool, June 1957.

Iodine Eruption Due to Estopen.—Dr. D. Freshwater.

A man aged 46. On 27 May 1957 this patient started a course of Estopen, 500,000 units daily for an attack of bronchitis. About 20 hours later he developed florid pyogenic granulomatous lesions of the face and arms.

Fig. 1.

On admission five days after the onset of the rash, and 24 hours after the drug had been withdrawn, neither iodide nor bromide could be detected in the urine, and there was no excess of either in the blood.

At this time the patient showed a moist granuloma spreading over the whole of the nose with scattered rather fleshy pustules on the forehead, chin and elbows (Fig. 1). The histology was typical of an iodide granuloma, and in spite of the absence of a history of iodine ingestion a diagnosis of iodine eruption was made. It was then discovered that Estopen is the hydriodide of the diethylaminoethyl ester of penicillin G. Sodium chloride, 1 g. t.i.d. was started on 4 June, and the rash cleared in a week. As a test a small dose of potassium iodide was given: this was followed by rapid

development of oedema of the face and neck, general malaise, pain in the joints and a temperature of 99·8 F., which subsided within 36 hours. At the same time the facial eruption relapsed and took a further twelve days to clear, being treated on this occasion with sodium chloride 3 g. t.i.d.

When the patient was seen six months later there was widespread superficial scarring of the nose, rather resembling a burnt-out lupus erythematosus.

The following case also was shown:

Leprosy.—Dr. F. Glyn-Hughes.

BOOK REVIEW.

The Biochemistry of Wool Lipoid.*

Anyone who becomes interested in the biochemistry of the skin cannot help being impressed by the number and variety of fatty substances, in the widest sense, occurring upon the surface of the skin. The constitution of these " fats " varies markedly in different species and while the subject is of great economic importance, it is remarkable that a book of nearly 400 pages has been written dealing with the lipides of one species.

However, in a way Dr. Truter has written two books: One dealing first in a straightforward fashion with the fleece, the chemical constitution of wool wax and of " suint ", as the cold water soluble components of the fleece are termed. After this it discusses certain aspects of the technology of wool wax—chapters on recovery, saponification and so on. Of their value to the wool chemist I am not competent to judge. They are however interestingly written and easy to read and give the impression throughout that the writer has first-hand knowledge of the processes he describes.

Interspersed between these chapters are some others which, while relevant to the main theme, will I think attract a wider public. These chapters form virtually self-contained essays on emulsions, on the isolation and determination of cholesterol and on lanostane and steroidal derivatives. One other chapter on the sorting of molecules by size and shape must I think be an account of one of Dr. Truter's own pet subjects. Certainly it is the best account of this process that I have come across so far. This method of approach of the problem of separation of components of a mixture is of course very recent—exemplified by the fact that 36 of the 43 references cited refer to publications of the past 10 years.

The biochemist interested in the skin will certainly find much to entertain and instruct him in this book. For the practising dermatologist it contains little of relevance to his everyday work. However, two of my clinical colleagues have had occasion to consult the review copy so that it would appear to be a necessity in any comprehensive dermatological library.

The book is attractively produced and well illustrated. I suppose we must school ourselves to think £3 a reasonable price for a moderately sized book these days.

A.T.

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* *Wool Wax*. E. V. Truter (1956). Cleaver Hume-Press. Pp. 368. Price £3 0*s*. 0*d*.

CURRENT LITERATURE.

EPOXY RESIN DERMATITIS. L. B. Bourne. (1957) *Practitioner*, **67**, 179.

These resins are used in electronics, engineering and other trades. They are used with catalysts of the aliphatic polyamine type because of their adhesive capacity.

At the site of contact unprotected workers show a punctate erythema which may become confluent. The spread is usually from the hands up to the forearms and, if the sensitization is of a high degree, an exfoliative dermatitis of the whole body with secondary sensitization and oedema of the face and eyelids is likely; occasionally bullae develop on the arms. Resin splashes harden on the skin and removal causes much local trauma. The onset of symptoms may develop within fifteen minutes of exposure or may be delayed for many weeks.

The "no touch technique" should be employed in handling these materials, and where there is risk of exposure to volatile material mixing must be carried out in a fume cupboard.

R. J. C.

ADVANCES IN THE TREATMENT OF SKIN DISEASES. O. L. S. Scott. (1957) *Practitioner*, **387**, 179.

Prednisone and prednisolone are now used more commonly than cortisone and corticotropin in treating serious disorders such as pemphigus, systemic lupus erythematosus, dermatomyositis and sarcoidosis. These hormones are occasionally justified in cases of severe and intractable eczema.

Chloroquine and steroids appear to act synergistically in some cases of systemic lupus erythematosus. Chloroquine alone is useful in chronic discoid lupus erythematosus, actinic dermatitis and polymorphic light eruption.

The use of drugs influencing pigmentation, "tranquillizers", antibiotics, sulphones, sulphonamides and physical agents, including Grenz rays, are also discussed. R. J. C.

THE LIVEDOS. D. Griuspan and A. Zurita. (1957) *Arch. argent. Derm.*, **7**, 153.

When people have used the word livedo, what have they had in mind? The authors have read the literature, studied the relevant physiology and pathological anatomy, and defined the term as skin of a livid or cyanotic colour arranged either in a netlike or arborescent pattern arising from deficient oxygenation of blood and depending on anatomical or functional changes in the blood vessels of the skin. This definition excludes erythema ab igne and some rare conditions that have been grouped with the livedos. There is a sharp division between the functional and the organic. Cutis marmorata, although at times it may become more or less permanent, is a functional example with no particular histological features. It is the physiological network exaggerated and made visible by cold. Typical organic types are livedo racemosa described by Ehrmann in syphilitics, with lesions in the arteries, and the livedo reticularis of Adamson with lenticular lesions and pathological changes in the veins. All other genuine livedos fall between these two extremes. G. W. B.

PANNICULITIS OF THE WEBER-CHRISTIAN TYPE WITH SARCOID HISTOLOGY. J. Kriner. (1957) *Arch. argent. Derm.*, **7**, 125.

A woman aged 47 had had recurrent attacks of panniculitis over several years and the earlier attacks had left typical cicatricial depressions. A section of a recent lesion showed in the hypodermis round masses of epithelioid cells and a few giant cells surrounded by a zone of lymphocytes: in adjacent areas the histological changes were those usually found in this affection.

G. W. B.

BESNIER'S PRURIGO AND URTICARIA IN BRONCHIAL ASTHMA. Sven Bergman. (1957) *Acta allergologica*, **11**, 193.

Besnier's prurigo occurred in 4·5% of 378 patients with bronchial asthma, the incidence being higher in patients whose asthma began before the age of 20, and greater in males than in females. Extrinsic allergens were considered important in 7 out of 9 men, and 6 out of 8 women who suffered from the two conditions. Urticaria occurred in 13·4%, the sex distribution being equal.

H. T. H. W.

DISTRIBUTION OF GAMMA GLOBULIN GROUPS IN SERA FROM PATIENTS WITH ALLERGY AND PSORIASIS. Sven Bergman. (1957) *Acta allergologica*, **11**, 200.

The sera from patients with bronchial asthma, hay fever, Besnier's prurigo, urticaria, and psoriasis gave normal distribution of gamma globulin groups. H. T. H. W.

POLYPOSIS OF GASTRO-INTESTINAL TRACT : THE PEUTZ SYNDROME. David Bailey. (1957) *Brit. med. J.*, ii, 433.

Four new examples of multiple adenomata of the gastro-intestinal tract with melanin pigmentation of the oral mucosa, lips and face are reported and the literature about this condition (Peutz syndrome) is fully reviewed. S. T. A.

CROSS SENSITIZATION OF THE FEET AND HANDS DUE TO CHROME TANNED LEATHER SHOES AND GLOVES. G. E. Morris. (1957) *New Engl. J. Med.* **257**, 567.

An eruption on a nurse's feet and one which appeared on her hands after wearing leather gloves was traced to the chromium salt used in tanning the leather, basic chromium sulphate.

A patch test with a 0·2% solution of this substance was strongly positive.

After a long period of freedom, wearing leather shoes for two days caused a recurrence on both hands and feet. A. D. P.

MELANIN PIGMENTATION AND ITS ENDOCRINE CONTROL. S. Deutsch and H. Mescon. (1957) *New Engl. J. Med.* **257**, 222.

The anatomy, physiology and biochemistry of melanin pigmentation in man is widely reviewed and many references are given.

Particular attention is paid to the possible role of the pituitary in the synthesis of melanin and it is suggested that there may be more than one substance in the pituitary with melanophore stimulating activity. A. D. P.

A STUDY OF HEREDITARY HAEMORRHAGIC TELANGIECTASIA. R. M. Bird. J. F. Hammarsten, R. A. Marshall and R. R. Robinson. (1957) *New Eng. J. Med.*, **257**, 105.

Study of a family in which 32 of 170 members had hereditary haemorrhagic telangiectasia is described. The disorder was transmitted as a simple dominant, and linkage with certain blood groups was sought for but not found. Symptoms, of which epistaxis was far the commonest, appeared chiefly in the third and fourth decades. Lesions were most often seen on the face and then on the lips, nares and tongue, in that order. A. D. P.

THE ATTRIBUTABILITY OF INFECTIOUS DISEASES OF THE SKIN. W. Gertler and H. Gartmann. (1957) *Berufsdermatosen*, **5**, 149.

This is a very detailed discussion of common and rare infectious diseases which may under certain conditions and in certain occupations be regarded as occupational disorders and therefore entitle the sufferer to industrial benefits. W. G. T.

THE STRUCTURE OF BASES IN TOPICAL APPLICATIONS IN DERMATOLOGY. H. E. Kleine-Natrop. (1957) *Berufsdermatosen*, **5**, 165.

The author is concerned with the lack of definition in the terminology of substances used for external application in dermatology. This difficulty gives rise to a great deal of misunderstanding in the assessment and discussion of treatment in skin diseases.

The author proposes a new classification suggesting that basic materials are either solid fluid or fatty and that a great number of combinations are possible. With the help of an isosceles triangle each corner of which represents one of the consistencies he creates 66 varieties of consistency which should go a long way to help out of the present difficulties. W. G. T.

ON TYPICAL CHANGES OF LIPOID AND PENTOSE CONTENTS OF EXTRACTS OF THE HORNY LAYER IN VARIOUS OCCUPATIONAL DERMATOSES. H. Buckup and A. Szakall. (1957) *Berufsdermatosen*, **5**, 181.

The elasticity of the horny layer and its capability of resisting mechanical trauma depends on its water content. Recent work has shown that chemically the hygroscopic material consists mainly of purines, aminoacids and pentose. It was also found that lipoids are not fixed but freely mobile.

Pentose and lipoid contents of skins of patients who had suffered from choracne, cement dermatitis and dermatitis from solvents in the past were examined and the values obtained compared with those from skin of normal persons. In chloracne and cement dermatitis the values were higher both for lipoids and pentose, in solvent dermatitis lipoids were normal and only pentose values were raised.

Since investigations were not carried out in acute cases it could not be stated whether the abnormal findings were the result of disease or caused by a congenital abnormality of the skin. This question will have to be determined. The investigations may however help to assess the suitability of workers for jobs in which they are in contact with irritants and in cases of resolved dermatitis whether the claimant is likely to have suffered from an industrial disease.

W. G. T.

EXPERIMENTAL INVESTIGATIONS WITH A DETOXICATING BARRIER CREAM. H. von Czetsch-Lindenwald. (1957) *Berufsdermatosen*, **5**, 191.

Up to the present barrier creams have had only a defensive action. They are either hydrophil or hydrophobe. Jäger was the first to attempt an offensive policy ; he incorporated tannins which blocked the receptive skin proteins and rendered them incapable of reacting with more dangerous substances. Polymeric phosphates have a similar action and have been used by the author in barrier creams to prevent damage particularly by heavy metals. The experiments showed that a local application of this type impeded fixation of metal ions and fat soluble and other dyes in the skin and facilitated the removal of such noxious agents. W. G. T.

ALLERGIC DERMATOSES DUE TO OCCUPATIONAL CONTACT WITH CHOLINE BROMIDE AND NITROSO METHYL UREA. F. Saynisch. (1957) *Berufsdermatosen*, **5**, 197.

Report of a case of choline bromide dermatitis in a woman working in a chemical factory and of a case of nitroso methyl urea dermatitis occurring in a laboratory assistant.

W. G. T.

COMPLICATIONS IN THE ORIGIN AND COURSE OF INDUSTRIAL DERMATOSES. A. M. Memmesheimer. (1957) *Berufsdermatosen*, **5**, 209.

It is often difficult to answer the question why the eczematous process caused by contact with irritants at work does not subside when the patient avoids the irritants and finds fresh employment. Minor and continuous trauma is thought to favour the entry of pyogenic organisms which causes a microbic eczema, or autosensitization may occur. In other cases the monovalent sensitization becomes a polyvalent one and unsuspected irritants often encountered away from work may be the cause of the persistence of the dermatitis. Another common cause is fungous infection and there are two tables showing the frequent incidence of this infection in various occupations. Some stress is laid on the possibility of psychological factors influencing the origin and persistence of occupational dermatoses. Some authorities deny the existence of occupational dermatitis altogether and consider the condition to be a psychogenic eczema. Contact dermatitis was well recognized before the era of social security but its extent was insignificant. The considerable publicity the subject has received as the result of factory legislation may act as a strong suggestive factor. Often the condition may be kept going by a desire to leave an uncongenial job or one to which the patient feels he is not fitted. The number of artefacts encountered in insurance work is extremely small but appears to be on the increase. The authors believe however that psychological factors are not often responsible for the persistence of industrial dermatitis. A certain number of cases are the result of the use of unsuitable local applications and sometimes caused by medical attendants. W. G. T.

DOUBTFUL SKIN DAMAGE BY A FLUORIC ACID COMPOUND. W. Braun. (1957) *Berufsdermatosen*, **5**, 231.

A workman was accidentally sprayed with a wood preservative containing ammonium bifluoride. Eight days later infiltration of the skin in various places was observed, also where no contact could have been possible. Eight months later a diagnosis of localized scleroderma was made and the possibility of an occupational origin denied because of the transient contact, the low concentration, and the early removal of the irritant and the development of the lesion at a much too early date after the contact. The possibility of scleroderma developing after trauma definitely exists, but reported cases usually developed months or years after the injury.

W. G. T.

ALLERGIC CONTACT DERMATITIS DUE TO TROPICAL TIMBER. K.-H. Schulz. (1957) *Berufsdermatosen*, **5**, 238.

Since the introduction of tropical timber for use in various industries cases of skin damage have been reported on many occasions. In each case the skin reaction appears to have been an allergic one since only a small proportion of workmen in contact with the wood were affected, lesions appeared only after a latent interval of some days to many months and skin tests were positive. Forty different tropical woods have so far been found capable of causing dermatitis. The author has investigated 3 carpenters who developed dermatitis 8–10 days after working with iroko, an African wood similar to teak. Two of the workmen had previously used the timber with minor skin manifestations developing.

Skin testing showed positive reactions with iroko, but not with teak. Tests with 1% chlorophorin, a phenolic resin first isolated from iroko in 1949, were also strongly positive. Chlorophorin is chemically related to toxicodendron (poison ivy) and cardol obtained from the Japanese lacquer tree. W. G. T.

FUNGUS PROBLEMS IN AN INDUSTRIAL PRACTICE. P. Hansen and H. Rieth. (1957) *Berufsdermatosen*, **5**, 244.

In the course of just over two years the authors reduced the incidence of tinea pedis in a large rubber factory from 75% to 40% of those employed. As causes of the ever-increasing number of cases of fungous infection communal bathing facilities, inadequate personal hygiene and increasing use of antibiotics are mentioned. Action taken consisted in hygienic measures in the factory education of the workmen and proper treatment of the condition. Particular importance is placed on the use of specially designed tiles for the floor of wash rooms and the spraying of these after use with an antiseptic solution. Instruction of first aid personnel and workmen as well as collaboration with hospitals treating the patients contributed to the success. W. G. T.

SKIN HISTAMINE AND INFLAMMATORY REACTIONS. L. Craps and Th. Inderbitzen. (1957) *Arch. belg. Derm. Syph.*, **13**, 1.

HISTAMINE IN NORMAL AND ABNORMAL HUMAN SKIN. L. Craps and Th. Inderbitzen. (1957) *Arch. belg. Derm. Syph.*, **13**, 113.

The first article deals with the histamine content of the skin in rats and guinea-pigs at intervals after freezing with ethyl chloride. The amount present depends on two factors : the reaction to the injury which leads to liberation of histamine and thus a reduction in the amount present in the skin and a subsequent increase of histamine as a result of cellular infiltration of the skin. These two factors vary according to the species of animal used.

The second article deals particularly with the human skin. The histamine content of the normal skin varies from region to region. It is highest in the head and neck, especially the eyelids. Care must be taken in assessing the histamine content of the skin after local anaesthesia especially with drugs of the procaine group It is lowered by their action. In pathological conditions the histamine content is proportional to the amount of cellular infiltrate in the dermis, especially if this consists of mixed cells. A purely lymphocytic infiltrate increases but little the histamine content of the skin. J. K.

CONSTITUTIONAL FACTORS IN ACNE VULGARIS. Albert Damon. (1957) *Arch. Derm., Syph., Chicago*, **76**, 172.

Out of 400 white American soldiers 40% showed a greater or less degree of acne vulgaris. The subtitle to the article " prevalence in white soldiers and lack of association with ancestry, complexion, body hair, blood group, handedness, plasma pepsinogen and physique " is a good summary of the findings. J. K.

THE RELATIONSHIP BETWEEN ACNE AND HAIR GROWTH. R. N. R. Grant. (1957) *Arch. Derm. Syph., Chicago*, **76**, 179.

It has long been noted that hairs are not seen issuing from follicles blocked by comedones. If the contents of a comedo are examined a fine hair or hairs will be found. If the hair can penetrate the mouth of the follicle and so keep up drainage of its contents, no comedo will form.

Secondary infection may destroy the follicle and if part of the sebaceous gland is spared but sealed off a cyst may form. J. K.

DOES THE TANNED SKIN PREVENT ERUPTION OF PITYRIASIS ROSEA ? Joseph V. Klander. (1957) *Arch. Derm. Syph., Chicago*, **76**, 200.

The author's answer is " no ". Pityriasis rosea affecting only untanned areas such as the " bathing drawers " area and axillae is fortuitous and is an example of localized eruption which is known to occur.

(The abstractor still feels that though the answer is in general correct, in some cases tanning can prevent the skin from becoming affected. He is unable to say why.) J. K.

THE MUCOCUTANEOUS END-ORGAN. R. K. Winkelmann. (1957) *Arch. Derm., Syph., Chicago*, **76**, 225.

That the mucocutaneous junctions are extremely sensitive is well known and the author shows that they possess a common and specialized end-organ. The morphological characteristics of this end-organ may account for the acuteness of the perception of touch in these areas.

J. K.

CONCOMITANT INFECTIONS WITH SYPHILIS AND TUBERCULOSIS IN EARLY CHILDHOOD —REPORT OF TWO CASES. R. V. Rajam and P. N. Rangiah. (1956) *Ind. J. Derm. Venereol.*, **22**, 101.

A child aged 2 with acquired muco-cutaneous syphilis had bone lesions which became much worse when the syphilis was treated. A cold abscess appeared from which tubercle bacilli were isolated and complete healing followed anti-tuberculous therapy.

An infant aged 10 weeks with congenital syphilis also had bone lesions which became worse after treatment and cleared with anti-tuberculous treatment. There was also a primary complex in the lung. An excellent discussion follows on congenital tuberculosis and reasons are advanced for considering this child to have had both congenital syphilis and congenital tuberculosis.

R. D. S.

TUMOURS OF THE VASCULAR SYSTEM WITH SPECIAL REFERENCE TO MALIGNANT ANGIO-ENDOTHELIOMA. D. J. Reddy, K. Gopalakrishniha Gupta, T. Suryaprakasa Rao, K. R. Venkiah and N. Venkataswamy Naidu. (1956) *Ind. J. Derm. Venereol.*, **22**, 165.

The authors pool their experience of vascular tumours over 2 years and discuss the difficulty, both clinical and histological, of deciding which are benign and which malignant, that is until the metastases appear. The aetiological role of trauma is stressed. R. D. S.

DIAGNOSIS OF CUTANEOUS MELANIN PIGMENTATION. Suresh S. Jhaveri and Sharat C. Desai. (1956) *Ind. J. Derm. Venereol.*, **22**, 183.

A detailed review of this subject. R. D. S.

SOME CUTANEOUS DISORDERS RELATED TO MALNUTRITION. C. Gopalan. (1957) *Ind. J. Derm. Venereol.*, **23**, 1.

Phrynoderma is " characterised by marked and extensive hyperkeratosis of the hair follicles, in which the hair follicles are surmounded by horny plugs, the issuing hair is distorted or absent, and the skin intervening between the follicles is also rough and dry ". A deficiency of essential unsaturated fatty acids is the main cause.

Crazy Pavement Dermatosis, the main skin change in kwashiorkor, is probably due purely to lack of protein in the diet, but vitamin B_2 deficiency may also play a part. The lesions are seen on the flexor surfaces where there is hyperpigmentation followed by central desquamation and hypopigmentation.

Dyschromatrichia is also found in kwashiorkor and is related to lack of protein. The hair is a brownish or sometimes reddish colour. Its cystine content is low, but there is no exact correlation between the loss of blackness and the loss of cystine. R. D. S.

PSEUDO-ANODONTIA ASSOCIATED WITH ECTODERMAL DYSPLASIA. D. J. Reddy and Y. Ramachandra Reddy. (1957) *Ind. J. Derm. Venereol.*, **23**, 70.

" Pseudo " because teeth were present but unerupted at the age of 15. Other changes : complete lack of hair, coarse dry skin which does not sweat, square hands and feet with clubbing, thick lips, optic atrophy, cysts in the lung, and umbilical hernia. Intelligence is normal.

R. D. S.

ENDOCRINE FACTORS IN HERPES GESTATIONIS. F. Gianotti. (1956) *Giorn. ital. Derm. Syph.*, **97**, 61.

The author studied 9 cases. He believes that there is evidence of endocrine dysfunction in these patients. They are often of masculine build and hairy, have scanty periods and are given to aborting for no clear reason. The altered urinary corticoid excretion, pigmentation and occasional hyperthyroidism suggest an imbalance or derangement of hypophyseal function. The author gives large doses of oestrogen, progesterone, or both, and claims dramatic results.

The table of extensive biochemical and endocrine investigations carried out on these cases is worth studying. D. S. W.

DERMATITIS OF RICE WORKERS DUE TO SCHISTOSOMIASIS. F. Gianotti. (1956) *Giorn. ital. Derm. Syph.*, **97**, 19.

The author demonstrates that the papular and pustular eruptions occurring on the legs and arms of rice workers is due to a schistosoma.

(Not likely to be a diagnostic problem in England, but the photographs show cercerial penetration of the skin well.) D. S. W.

THE STRUCTURE OF THE HAIR-ROOT SHEATH. V. Puccinelli. (1956) *Giorn ital. Derm Syph.*, **97**, 1.

The author has examined by polarized light the cuff that comes away with hairs pulled out in certain conditions of the scalp—notably pseudopelade. There are three layers, refracting differently, and a space between the cuff and the outer layer of the hair itself. He examines the changes that take place under the influence of various agents. D. S. W.

HAEMANGIECTASIA HYPERTROPHICANS (KLIPPEL-TRENAUNAY—PARKES WEBER). R. Cavalieri. (1956) *Cronache dell'Idi*, **11**, 5.

A report of four cases, three involving a leg, one an arm. In all there was evidence of an arteriovenous aneurysm. The relationship of this to the other components of the syndrome, the capillary naevus and hypertrophy of all the structures of the limb, is discussed.

D. S. W.

HEREDITARY SYSTEMATISED ELASTOSIS (PSEUDOXANTHOMA ELASTICUM). R. Cavalieri. (1956) *Cronache dell'Idi*, **7–8**, 146.

Over 300 cases have now been described. In three-quarters of these the skin changes are evident before thirty years of age. Rather more women than men are affected. In a review of 183 cases associated vascular lesions such as aortitis, aneurysm, arterio-sclerosis and juvenile hypertension were present in 34. It seems, therefore, that the presence of such lesions should be looked for diligently in every case. Out of 238 cases investigated by Touraine, 114 occurred in 49 families. But the method of inheritance is not yet agreed. Some believe it to be transmitted as an irregular dominant; sometimes it appears to be recessive. Diabetes has been recorded in association with this syndrome and—rather curiously—osteitis deformans in eleven cases. But it has recently been pointed out that Paget's disease is found in 3·7% of all post-mortems.

The author presents three cases which he has investigated fully.

This is a very long article which includes everything important that is known about this condition; it appears that the presence of angioid streaks converts it into the "Groenblad-Strandberg syndrome". D. S. W.

THE PROBLEM OF CUTANEOUS BLASTOMYCOSIS. L. Pfleger and H. Tirschek. (1957) *Dermatologica*, **114**, 1.

This longish, well-written and critical study of so-called blastomycosis of the skin points out clearly the difficulties and uncertainties which have to date made impossible the formulation of a satisfying classification or terminology. The number of species and even genera of fungi, many of them previously unknown as pathogens, shown to be the cause of skin lesions is rapidly increasing, but the clinical manifestations are remarkably similar in most cases, regardless of the causative organism. The histological picture is a curious mosaic of acute and chronic inflammatory and granulomatous changes, with foci of necrobiosis, and, paradoxically, this absence of specificity is almost pathognomonic. It should at least raise the suspicion of blastomycosis. The authors' own case was caused by an organism which rejoices in the name of "sporobolomyces salmonicolor Kluyver and van Niel", J. F. S.